Effects of Topical Emollient Therapy on Infants at or Less than 27 Weeks' Gestation

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Objective: To evaluate the effects of topical emollient therapy on fluid intake, urine output, serum electrolytes, glucose, bilirubin and other outcome measures of neonates ≤27 weeks' gestational age (GA) with birthweight (BW) <1,000 g.

Methods: We reviewed medical records of 18 infants treated with topical emollient Aquaphor®, and 36 BW- and GA-matched control infants that were not treated with similar topical emollient.

Results: Characteristics of the study and control infants were similar: BW: 698 ± 144 g vs. 732 ± 134 g, GA: 25.5 ± 1.3 weeks vs. 25 ± 1.6 weeks and Score for Neonatal Acute Physiology (SNAP) 14.3 ± 5.1 vs. 14.6 ± 7.8, respectively. Fluid intake was lower and urine output was significantly better in Aquaphor-treated infants during the first two weeks of life. Peak serum potassium and bilirubin values were also lower in the study infants. Insulin use, patent ductus arteriosus (PDA), intraventricular hemorrhage (IVH), retinopathy of prematurity (ROP), sepsis and duration of ventilator/oxygen use were similar among the groups.

Conclusion: Infants ≤27 weeks' gestation who had Aquaphor applied to their skin from birth required less fluids and had better urine output. These infants had lower serum potassium and bilirubin values during their first two weeks of life. Therefore, we conclude that topical Aquaphor application to the skin is beneficial for fluid and electrolyte balance in extreme preterm infants.

Key words: infant health ■ dermatology

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Preterm infants incur high losses of heat and insensible water due to a ratio of large surface area to body weight. Extreme preterm infants may have insensible water losses in excess of 100 cc/kg/day due to immature skin, larger exposed surface area and lack of subcutaneous tissue.[1,2] Often by two weeks of life, there is a rapid maturation of the epidermis postnatally. This makes the first two weeks of life very critical in this group of preterm infants. It is estimated that at 23–28 weeks' gestational age (GA), the epidermis is poorly developed, only 2–3 cell layers thick, with little development of the stratum corneum.[1] As a result of the skin's immaturity, there are high transepidermal water losses that lead to hypothermia and problems with fluid balance, as well as skin trauma leading to infection.[1-5]

Preterm infants require a stable thermal environment to minimize heat and insensible water losses. Current nursery care provides an adequate environment using plastic shields or blankets, incubators, headcaps and topical emollients.[1,2,6] Different methods of preventing insensible water losses have been investigated in the past 10–20 years. This research has ranged from topical emollients (Aquaphor® Eucerin®, petrolatum mixtures) and thermal blankets to Tegaderm® placed directly on the infant's skin.[3,4,6-12]

In 1981, Rutter et al. showed that skin water losses were reduced by 40–60% after one application of a petrolatum topical agent.[3] In 1996, Nopper et al. concluded that topical therapy with Aquaphor ointment decreased skin water losses for six hours after one application and reduced incidence of bacterial colonization of axillary skin. The limitations of this study were that: 1) the study group included infants <33 weeks' gestation and birthweight <1,500 g, rather than target the group of infants <28 weeks' gestation, when lack of epidermal development is more of a problem; 2) clinical aspects of electrolyte balance were not part of the study.

After reviewing an article by Nopper et al.,[11] the neonatal intensive care unit (NICU) at our institution began the practice of applying Aquaphor topical emollient in January 1997 to all of our preterm, very-low-birthweight infants. To evaluate the effects of Aquaphor therapy on fluid requirements, serum electrolytes and other outcome measures in neonates ≤27 weeks' gestation, we conducted the following study.

METHODS

This retrospective chart review was conducted at a level-3 nursery in central Texas. After reviewing the study by Nopper et al.,[11] the nursery at this institution began practice of topical application of emollient (Aquaphor, Beiersdorf Inc., Norwalk, CT) to extremely-low-birthweight infants. Aquaphor ointment contains petrolatum, mineral oil, ceresin and lanolin alcohol. As per the manufacturer's product information, Aquaphor contains no fragrances or preservatives that can irritate sensitive skin. Emollient was applied topically every six hours during the first two weeks of life to the entire body surface area of the infant, including face and scalp. Precautions were taken to avoid contact with infant's eyes. The ointment was supplied in individual tubes prepared by our children's pharmacy and allocated to each patient. The application of the ointment was charted appropriately in the patient's electronic medical record by nursing staff, as a medication.

Prior to the institution of Aquaphor use, infants were kept under plastic wrap to decrease insensible water loss, and other topical applications such as Eucerin were used as necessary for skin care. Plastic wrap covers were not used for infants receiving the Aquaphor therapy.

SUBJECTS

Study Infants

The following inclusion criteria were used to identify study infants: gestation ≤27 weeks, birthweight <1,000 g, survival to discharge, received Aquaphor topical emollient therapy every six hours during the first two weeks of life. Eighteen such infants were identified during 1997.

Table 1. Characteristics of control and study infants

Characteristic	Control Infants (N=36)	Study Infants (N=18)
GA (weeks)	25 ± 1.6	25 ± 1.3
Birthweight (g)	732 ± 134	698 ± 144
African-American (%)	15 (42)	8 (44)
Cord venous pH	7.32 ± 0.09	7.37 ± 0.05
Cord arterial pH	7.28 ± 0.09	7.29 ± 0.15
SNAP	14.6 ± 7.8	14.3 ± 5.1
Vaginal delivery (%)	19 (53)	9 (50)
Preeclampsia (%)	8 (22)	4 (22)
Prenatal steroids (%)	21 (58)	9 (50)

Values with ± represent mean ± SD; Differences between the groups not statistically significant

Control Infants

For each study infant, two control infants were identified with birthweight within 100 g and gestational age within one week. Thirty-six such control infants were identified that were born in 1995 and 1996 with gestational age ≤27 weeks' gestation, birthweight <1,000 g and survived to discharge. These infants did not receive topical emollient therapy with Aquaphor. These infants received other topical creams such as Eucerin as a necessity for dry skin only. Infants with <23 weeks' gestation, significant congenital anomalies or death prior to discharge were excluded.

Fluids and Electrolytes

An infant's fluid management was generally based on body weight, urine output, serum electrolytes and glucose values. Fluids calculated in the study included intravenous hyperalimentation fluid, other intravenous fluids and enteral feeds. Blood products were not included in the calculation. All potassium samples were drawn via arterial line or by venous puncture.

Data collection for both the study and control groups included the following: birthweight; gestational age; race; resuscitative measures taken at delivery; cord arterial pH; cord venous pH; Score for Neonatal Acute Physiology (SNAP) scores; use of dopamine/dobutamine; insulin use; steroid use for chronic lung disease; duration of ventilator and oxygen therapy; evidence of patent ductus arteriosus (PDA), intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL) or retinopathy of prematurity (ROP); the number of episodes of sepsis with positive blood cultures; and weights on day 7, day 14 and at discharge. Fluid status and electrolyte balance were compared and determined by the following: intake (cc/kg/day), output (cc/kg/hr), serum levels of sodium, potassium, glucose and bilirubin. All values were recorded and compared from day 1 to day 7 and day 14 of life between the two groups.

Statistical Analysis

Mean and standard deviations were calculated where appropriate. To compare continuous data between the study and control infants, a t test was used and to compare categorical data, Chi-squared and Fischer exact tests were utilized, and a P value <0.05 was considered significant.

RESULTS

Analysis of the study and control infants revealed similar mean birthweight, gestational age, cord venous pH, cord arterial pH and SNAP scores (Table 1). SNAP scores measured the severity of illness and results indicated that the study and control infants were equal in terms of degree of illness. Length of stay, and weights on day 7, day 14 and at discharge were similar (Table 2). Other data compared include insulin use; incidence of PDA, ROP and IVH; episodes of sepsis; duration of oxygen use; and the ventilator (Table 2). These results did not reveal any statistically significant results. Fluid intake, urine output, peak serum glucose, sodium, potassium and bilirubin mean values are shown in Table 3. There was a statistical difference in fluid intake on day 1 of life between the study and control groups. Study infants required 95 ± 34 cc/kg/day on the first day of life, whereas control infants requirements averaged 135 ± 52 cc/kg/day ($P<0.005$). In addition, fluid intake was statistically significant on the sixth day of life (151 ± 20 cc/kg/day vs. 169 ± 36 cc/kg/day, $P=0.049$) and the seventh day of life (138 ± 39 cc/kg/day vs. 158 ± 32 cc/kg/day, $P<0.04$). On days 2 and 14 of life, results were statistically significant for output measurements between the study and control groups. On day 2, urine output was 4.8 ± 1.8 cc vs. 3.6 ± 2.1 cc/kg/hr ($P<0.04$) and on day 14, 4.1 ± 2.0 cc/kg/hr vs. 3.0 ± 1.4 cc/kg/hr ($P<0.02$) between study infants and control infants, respectively. Mean peak glucose and sodium values between the study and control infants did not show any statistical difference. On day 5 of life, there was a statistical difference in mean peak potassium values between the study infants (3.9 ± 0.4 mEq/dl) and the control (4.4 ± 0.4 mEq/dl), with a P value of 0.01. Bilirubin values for the second and third days of life were statistically significant between the study and control groups. On day 2 of life, the study infant's mean bilirubin values were 5.2 ± 1.3 mg/dl compared to 6.3 ± 2.1 mg/dl in the control group ($P=0.049$). On day 3 of life, the study infant's bilirubin values were 4.4 ± 1.2 mg/dl compared to 5.5 ± 1.9 mg/dl in the control group ($P=0.026$).

DISCUSSION

When Aquaphor was applied to their skin, extremely-preterm infants required less fluids and had better urine output. Also, their serum potassium and bilirubin values were lower during the first two weeks of life. Fluctuations in glucose and sodium values were minimal and the values were lower in treated infants, compared to controls, but differences did not reach statistical significance. We believe glucose values were lower because these infants required significantly lower volumes of fluid. Sodium and bilirubin values were lower due to better hydration status.

Nopper et al.[11] proved that there were effective reductions in transepidermal water losses with topical emollient therapy, but the fluid intake was similar in both groups. This was probably due to the initial time lag for the subjects to enter the study (approximately 96 hours) and the relative maturity of infants in the study (mean birthweight and GA were approximately 1,200 g and 29 weeks, respectively). Pabst et al.[12] found that fluid intake was higher in the control group compared to the Aquaphor group, even though it did not reach statistical significance ($P=0.08$). There were only 11 infants in the study group and eight control infants in this study, and the infants were relatively more mature with a mean birthweight of 1,011 g to 1,143 g and a mean GA of approximately 28 weeks. In our study, infants are more immature with a mean GA of 25 weeks with a mean birthweight near 700 g. It appears that benefits of Aquaphor on fluids and electrolytes are more pronounced in lower-birthweight and younger-GA infants. Hypernatremia, hyperkalemia and hyperbilirubinemia are common problems in these small preterm infants, hence the inclusion of these factors in our study. Other studies[11,12] did not include all electrolytes and bilirubin as part of the evaluation.

With an application of Aquaphor every six hours to the skin of preterm infants, we did not witness any toxic or local reactions. We had more problems with cardiac monitor lead placement and temperature probes, as did Nopper et al.[11] Parents became involved in the application of the emollient and

Table 2. Comparison of morbidity of study and control infants

Characteristic	Control Infants (N=36)	Study Infants (N=18)
Intubation in delivery room (%)	31 (86)	18 (100)
Dopamine/dobutamine use (%)	11 (31)	9 (50)
Insulin use (%)	12 (33)	3 (17)
Duration of ventilator use (days)	25.8 ± 19.8	21 ± 14.8
Duration of oxygen use (days)	63.8 ± 38.4	55.3 ± 14.5
Steroids for chronic lung disease (%)	19 (53)	11 (61)
Patent ductus arteriosus (%)	26 (72)	12 (67)
Intraventricular hemorrhage (%)	14 (39)	5 (28)
Grade-3 or -4/PVL (%)	11 (31)	5 (28)
Retinopathy of Prematurity (%)	32 (89)	13 (72)
Stage-3 or -4 (%)	11 (31)	3 (17)
Episodes of sepsis (%)	10 (28)	3 (17)
Discharge weight (g)	2,460.6 ± 605	2,217 ± 344
Length of hospital stay (days)	93 ± 25.8	103.5 ± 18

Values with ± represent mean ± SD; Differences between the groups not statistically significant

Table 3. Comparison of study and control infants: fluids, glucose, electrolytes and bilirubin values

Day	Intake (ml/kg/day)		Output (ml/kg/hour)		Glucose (mg/dl)		Sodium (meq/dl)		Potassium (meq/dl)		Bilirubin (mg/dl)	
	+	–	+	–	+	–	+	–	+	–	+	–
1	95*	135	2.0	1.5	133	179	140	143	5.4	5.7	4.5	4.3
2	135	166	4.8*	3.6	120	157	145	148	5.2	5.6	5.2*	6.3
3	154	182	4.7	4.4	104	127	143	145	4.8	5.0	4.4*	5.5
4	161	166	4.6	4.1	112	111	140	140	4.5	4.6	4.5	4.8
5	169	180	4.3	3.8	125	112	136	136	3.9*	4.4	4.9	5.0
6	151*	169	3.8	3.5	122	123	136	138	4.1	4.2	4.9	4.9
7	138*	158	3.8	3.1	118	125	138	136	4.5	4.4	5.0	5.2
14	141	142	4.1*	3.0	123	122	138	138				

+ Infants received topical Aquaphor therapy; - Control infants; * Values represent statistical significance with $p<0.05$

seemed to look forward to those times in the day. The practice of topical emollient therapy may have encouraged bonding between parents and infants, at a time that is frightening and creates much anxiety during a NICU stay. The strength of this study is that it has a relatively large number of infants in the lowest-birthweight category, compared to the previous studies. The study limitations are its retrospective nature and its use of historical controls.

In conclusion, infants ≤27 weeks' gestation who had the Aquaphor emollient applied to their skin from birth required less fluids, had better urine output, more stable electrolytes and lower bilirubin values during their first two weeks of life. Therefore, we conclude that the topical emollient cream, Aquaphor, applied to the skin of extremely preterm infants is beneficial, particularly for fluids and electrolyte management.

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